

Amendments to the specification

Please note that all page numbers and line numbers herein refer to the concurrently filed English language translation of the Japanese language specification.

Please amend the title as follows.

~~METHOD~~ METHODS OF TREATING ~~INFLAMMTORY~~ INFLAMMATORY
~~DISEASE~~ DISEASES ASSOCIATED WITH BONE DESTRUCTION

Please insert the following heading and paragraph at page 1, line 5.

Cross-Reference to Related Applications

This application is the U.S. national stage application of International Application Number PCT/JP2004/002887, filed March 5, 2004, which, in turn, claims the benefit of Japanese Patent Application Serial Number 2003-075964, filed March 19, 2003.

Please amend the paragraph starting on page 8, line 7, and ending on page 9, line 2, as follows.

The number of amino acids that are substituted, deleted, and/or added is usually not more than 15, preferably 11 or less, more preferably 9 or less, more preferably 7 or less, and more preferably 5 or less. Proteins comprising amino acids that are conservatively substituted tend to maintain their activity. Conservative substitutions comprise substitutions between amino acids within each of the groups, such as basic

amino acids (e.g. lysine, arginine, histidine), acidic amino acids (e.g. aspartic acid, glutamic acid), uncharged amino acids (e.g. glycine, asparagines, glutamine, serine, threonine, tyrosine, cysteine), nonpolar amino acids (e.g. alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), β -branched amino acids (e.g. threonine, valine, isoleucine), and aromatic amino acids (e.g. tyrosine, phenylalanine, tryptophan, histidine). Amino acid sequence identities can be determined by using, for example, the ~~BLASTP~~ BLAST program (Altschul, S. F. *et al.*, 1990, J. Mol. Biol. 215: 403-410). Specifically, blastp program may be used. For example, searches may be conducted using default parameters, switching off all filters including Low complexity, at the BLAST web page of NCBI (National Center for Biotechnology Information) (Altschul, S.F. *et al.* (1993) Nature Genet. 3:266-272; Madden, T.L. *et al.* (1996) Meth. Enzymol. 266:131-141; Altschul, S.F. *et al.* (1997) Nucleic Acids Res. 25:3389-3402; Zhang, J. & Madden, T.L. (1997) Genome Res. 7:649-656). For example, by using the BLAST 2 Sequences program (Tatiana A *et al.* (1999) FEMS Microbiol Lett. 174:247-250), which compares two sequences, an alignment of two sequences can be produced to determine identity between the sequences. Gaps are treated similarly to mismatches. For example, an identity value is calculated against the entire amino acid sequence of natural soluble FGFR or FGFR intracellular signal transduction inhibitory protein. Furthermore, in hybridization, probes are prepared from nucleic acids comprising the coding region of natural soluble FGFR or FGFR intracellular signal transduction inhibitory protein, or from nucleic acids subjected to hybridization, and these probes can then be used to

identify hybridization by detecting whether they hybridize to other nucleic acids.

Stringent hybridization conditions are, for example, hybridization in solutions comprising 5x SSC, 7% (W/V) SDS, 100 µg/ml denatured salmon sperm DNA, 5x Denhardt's solution (1x Denhardt's solution comprises 0.2% polyvinyl pyrrolidone, 0.2% bovine serum albumin, and 0.2% ficoll), at 48°C, preferably at 50°C, and more preferably at 52°C, followed by washing for two hours while shaking at a temperature equal to that of hybridization, preferably 60°C, more preferably 65°C, and most preferably 68°C.

Please replace the Sequence Listing found in the English language translation of PCT/JP2004/002887 with the enclosed paper copy of the Sequence Listing provided with the concurrently filed Statement Under 37 C.F.R. §§ 1.821 – 1.825.